REMARKS

I. Claims in the Case

Claims 20 and 88 have been amended. Claims 87 and 89 have been canceled. Claims 3, 4, 20, 21, 23-29, 36-76, 85-86 and 88 are pending.

II. Objection to Claim 20

Applicants have amended claims 20 to address the objection regarding "said first" and "said second" primer.

III. Rejections Under 35 U.S.C. §112, First Paragraph

The Action next rejects all of the pending claims under 35 U.S.C. §112, first paragraph, taking the position that various phrases used in the claims are not adequately described in the specification.

In response, Applicants would first note that the rejection is more properly one under 35 U.S.C. §112, second paragraph, but will respond nonetheless in order to progress the case towards allowance.

The Action first complains of the phrase "a predetermined 5' sequence", "a predetermined linker" and "wherein each member of the pair anneals to a different predetermined linker sequence." These phrases are found in claims 87-89.

To address this rejection, Applicants have amended claim 88 to remove the word "predetermined" as it appears that this phrase is surplusage. The term "predetermined" was initially employed simply to denote that fact that the linker sequence was a known sequence. This fact is believed to nonetheless be inherent in the claim and thus its scope has not in any way

been narrowed by this amendment. This amendment should adequately address the Action's section 112 concerns.

The Action also complains of the use of the term "random" in claim 20. Claim 20 has now been amended to clarify that two separate primer populations are employed, wherein the primer set populations have specificity regions such that the population collectively reflects all possible sequence combinations of A, T, G and C. Support for the amendments to claim 20 can be found at the top of page 21. As explained in the first two paragraphs of page 21, an aspect of the invention involves the use of a specificity region incorporating such a random population of sequences to ensure that there will always be a specificity region that will anneal to the target.

IV. Rejection of Claims 87-89 as Anticipated by Senapathy '058

The Action next rejects claims 87-89 as anticipated by the Senapathy '058 patent. As claim 87 has been canceled, Applicants will direct their comments to claim 88 and dependent claim 89.

In response, it is Appellants position that no proper *prima facie* rejection has been set forth by the Examiner with respect to the subject matter of claim 88, and, hence, dependent claim 89. It is noted that the claim is directed to a method of making a population of primer molecules, wherein the primer molecules of said population has (a) a 5' sequence that incorporates a sequence that anneals to the same linker sequence as other members of the population and (b) a random 3' terminal specificity region of from 3 to 8 nucleotides in length, such that the population of primer molecules have specificity regions collectively reflecting all possible sequence combinations of A, T, G and C, and wherein the 5' sequence of primer molecules of the first population anneal to a different linker sequence than do the 5' sequence of primer

molecules of the second population, and wherein the method includes incorporating a region that anneals to a linker into 5' region of the primer.

In contrast, the Senapathy patent appears to disclose in Figures 1 through 3, the concept of "genome walking with a known first primer and a partly fixed second primer." Similarly, Figure 4 refers to the use of the "same set of partly fixed second primers" all working from a known primer which does not appear to have "unfixed" regions. Thus, these embodiments appear to be distinct from the invention of claim 88.

In the subject Action, the Examiner fails to point to any teaching that anticipates the foregoing subject matter. Even if Senapathy does teach random sequences, the Examiner has already gone on record to observe that the phrase "random" sequence is not the same as "collectively reflecting all possible sequence combinations of A, T, G and C." Moreover, it is evident that the Senapathy primers anneal to the same sequence, not different sequences, thus, there is no teaching of two separate populations of primers wherein the primers of one population anneals to a different target sequence than do primers of the other population.

To further clarify the novel nature of the invention and to address the Action's concerns that the linker-annealing limitation is an intended use, Applicants have placed claim 88 into method format that includes the step of incorporating a sequence that anneals to a linker into the 5' region of the primer. Applicants have been unable to find any teaching in Senapathy that concerns incorporating a linker-annealing sequence into the 5' region of the primer.

V. Rejection of Claims 87-89 as Anticipated by Silver

The Action next rejects claims 87-89 as anticipated by Silver.

We respectfully disagree for the same reasons set forth above with respect to Senapathy, which are incorporated herein by reference. Furthermore, it is noted that the primers of Silver

that contain random specificity regions are shown ***not*** to have 5' regions that bind their template. For example, the Silver patent clearly discloses in Figure 1 that the region of ***its*** primers that is located 5' of the random sequence ***does not*** bind to the template. It is not until the Silver prepares a primer that does ***not*** incorporate a random sequence that it teaches the use of a known sequence that binds to the template. See, for example, bottom of Figure 1 as compared to the first two depictions at the top of Figure 1.

The Action's reference to col. 3, lines 55-57 of Silver, and its argument that the sequence 5'-GACTCNNNN-3' will, if provided a linker sequence of 5'-XXXXGAGTC-3', anneal thereto, is already commented upon above. This argument is unavailing as the Action fails to direct us to a teaching or suggestion of a linker that incorporate such a sequence. On the contrary, Silver teaches against such an embodiment since, as explained in the foregoing paragraph, the 5' regions of its primers that have random sequences at their 3' end do not bind to the template – only those primers that do not have random 3' sequence bind to the template.

Indeed, the Action relies upon the 5'-GACTCNNNN-3' of Silver, but admittedly fails to demonstrate that the complement of such sequence is found in any known linker. Furthermore, for the reasons explained above, it is believed that amendment of the claim to recite a method obviates the Examiner's "intended use" concerns.

VI. Rejection of Claims 87-89 as Anticipated by Senapathy '428

The Action next rejects claims 87-89 as anticipated by Senapathy '428, taking the position that Senapathy '428 teaches separate primer sets that meet all the limitations of the rejected claims, referring in particular to claim 25.

In response, Applicants incorporate the foregoing arguments with respect to Senapathy '058 and Silver. Again, Applicants have been unable to identify in Senapathy '428 any teaching or suggestion to incorporate a linker sequence annealing region into the 5' region of the primer population. Instead, the primers of Senapathy '428 appear to be designed to sequence "an unknown DNA of a given length." (col. 6, lines 1-2). A linker sequence, as explained, for example, at the bottom of page 8 of the specification, must be a known, characterized molecule that is ligated to the ends of a target molecule. Thus, in contrast to Senapathy, whose primers are for sequencing DNAs of unknown sequence, the primers of the present invention are designed to anneal to a known linker sequence that has been ligated to a target molecule. This is achieved by incorporating a linker-annealing sequence into the 5' region of the claimed primers.

For the foregoing reasons, it is submitted that the subject matter of claim 88 is both novel and non-obvious over the Senapathy '428 disclosure.

VII. Rejection of Claims as Obvious Over Senapathy '428 in View of Issaacs *et al.*

The Action lastly rejects the remaining claims as obvious over the combination of Senapathy '428 in view of Issaacs et al.

In response, Applicants have amended the presently rejected claims in a manner that the Examiner has previously indicated would distinguish over the combination of Senapathy '428 and Issaacs et al., by directing the first step of the base claim 20 to "preparing a DNA molecule by positioning a first linker sequence at one end of the DNA molecule and a second linker sequence, different from said first linker sequence, at the other end of the DNA molecule." This is believed to distinguish over the references in that neither reference teaches the concept of

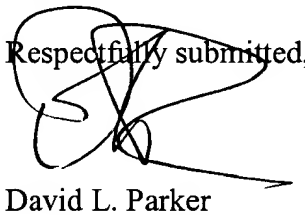
preparing such a DNA molecule and then fashioning primers that anneal to and prime off of such prepared DNA molecules.

VII. Conclusion

It is believed that in light of the foregoing the present case is in condition for allowance and favorable action thereon is earnestly solicited. If the Examiner has any questions, comments or recommendations, he is earnestly requested to contact the undersigned representative.

Please date stamp and return the enclosed postcard to evidence receipt of this document.

Respectfully submitted,



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